PATENT

Attorney Docket No.: 36290-0318-00-US (207195)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re:	Patent application of Jason Gordon Beith	:	Conf. No.: 9867
Serial No.:	10/524,612	:	Group Art Unit: 3774
Filed:	May 15, 2006	:	Examiner: Stroud, Jonathan R.
For:	Valve	:	

DECLARATION OF JASON GORDON BEITH UNDER 37 C.F.R. § 1.132

I, Jason Gordon Beith, declare the following:

1. I am the inventor of the invention described in U.S. Patent Application No. 10/524,612 ("the '612 application").

2. I am Vice President of Research and Development for AorTech Medical Devices (USA), Inc. ("AorTech"), a subsidiary of AorTech International PLC, the assignee of the '612 application. I have worked on the design and development of polymer heart valves and other biomedical devices for about the past eight years. My formal education is in Civil Engineering with specialization in earthquake engineering and structural dynamics, and prior to my biomedical device work, I was employed for several years designing and modeling structures to withstand extreme earthquake and wind environments.

3. This declaration is offered as evidence that a person having ordinary skill in the art with knowledge of all that Moe discloses would not have found it obvious to design the claimed invention.

4. I have reviewed the Examiner's rejection of claims 16-23 in the Office Action mailed on January 21, 2009 based on U.S. Patent Application Publication No. 2002/0082687 to Moe ("Moe"). I have reviewed the written description, figures, and claims of Moe.

5. Moe discloses an approach to designing leaflets for a heart valve that follows the conventional wisdom in the art. The resultant design disclosed by Moe has a similarly disadvantageous geometric configuration to other prior art valves designed by those working in this field for many years, which causes the valve leaflets to have problems of reduced durability and catastrophic failures. These problems are solved by the claimed valve leaflet design, which does not conform to the conventional wisdom.

6. The conventional wisdom in the artificial heart valve field, which was essentially dogma prior to the presently claimed valve, is that an artificial leaflet valve must look like (i.e., be configured and shaped like) a natural heart valve. Therefore, all of the prior art leaflet valves of which I am aware sought in one way or another to mimic or imitate the shape and functional characteristics of a natural tissue valve. Indeed, even though the '612 application has been published for over two years, those of ordinary skill in the field still have not appreciated or accepted the benefits of the claimed design, and continue to attempt to design artificial leaflet valves based on the criteria that have been established using the conventional wisdom.

7. The conventional wisdom in the field of artificial heart valves is an amalgamation of the expertise of prominent heart surgeons, physicians, and biomedical engineers who have worked for years to try to develop a viable polymer replacement for a natural heart valve. For example, some of the leading companies seeking to design and build artificial leaflet valves retain the prominent heart surgeons from around the world to consult on designs, and those surgeons perpetuate the dogma that an artificial leaflet valve must have the same physical shape and features as a natural tissue valve. Prior to me, nobody having ordinary skill in the prior art ever considered that the material from which artificial leaflet valves are made might not have the same functional capabilities as natural tissue.

8. A governing consideration in prior art valves designs was the need to have coaption. Coaption is the coming together of surfaces of each valve leaflet at the free ends of the leaflets in order to create a seal that substantially prevents regurgitation of blood flow backward through the closed valve. Moe exemplifies this concern for coaption and as a result designed each of the leaflets specifically to have a two-part coaption surface extending from the triple point (where the free edges of the three leaflets in a three-leaflet valve meet) to the commissure at each edge of the leaflet (where the sides of each leaflet join the support posts disposed between the leaflets); Moe explicitly states the need to have vertical surfaces at the upper portion of each of the leaflets for this very purpose. The other prior art valves of which I am aware also have been designed with a focus on optimizing coaption and therefore are formed to have vertical or near vertical surfaces at an upper portion of each leaflet.

9. Another governing consideration in prior art valve designs was the need for each leaflet to have a belly in the axial direction, because the belly was thought to be necessary to aid in sealing and to reduce static stress of the leaflet when the valve was closed. Moe exemplifies the focus on the leaflets having a belly; Moe explicitly sets forth that a "simple, singly curved leaflet belly" is one of the criteria that has been established in the art and states that such a belly is therefore a design parameter of the valve described therein. Moe at paragraph 0015.

10. It is my understanding that Moe accurately articulates some of the key design principles for artificial heart valves that were widely held and accepted at the time of my invention. Moe at paragraphs 0012 to 0017. These principles were quite rigidly adhered to in the field as essential in the design of such valves. Specifically, Moe emphasizes the (well accepted in the art) need for a bi-directionally curved leaflet having a belly and a near vertical coaption surface.

11. To meet the criteria that had been established in the prior art, Moe discloses a heart valve including a plurality of leaflets (preferably three). The leaflets disclosed by Moe

have curvatures defined by very specific geometric functions in both a lateral XY direction (i.e., perpendicular to blood flow) and an axial Z direction (i.e., parallel to blood flow). In particular, each leaflet includes a bottom portion and a top portion. The bottom portion is formed from a cylinder having an axis, a radius, and an axial section. The top portion has two sections. The first section of the top portion is defined by a first arc having a first radius swept along a first helix, the first helix being a right-handed helix and having the same radius and axis as the cylinder. The second section of the top portion is defined by a second arc having a second radius swept along a second helix, the second helix being a left-handed helix and having the same radius and axis as the cylinder. In a central belly, the bottom portion and the right and left sections of the top portion converge such that the left and right sections of the top portion extend generally axially from the belly to form generally axially oriented coaptive surfaces for sealing with adjacent leaflets when the valve is closed.

12. Every time Moe's valve leaflet opens or closes, the belly must invert, which creates tremendous dynamic stresses in the leaflet, resulting in concentrated locations of strain energy density that will render the Moe leaflets prone to failure.

13. Prior to the presently claimed valve, skilled artificial heart valve designers understood (or believed they understood) the highest stress position of a valve leaflet to occur when the valve was fully closed and resisting back pressure, and a secondary high stress position of a valve leaflet to occur when the valve was fully open to allow maximum forward flow. Therefore, prior skilled artisans determined leaflet shapes and thicknesses by static modeling at the fully closed and open positions.

14. Prior art leaflet valves made from polymer materials have been routinely prone to premature failures which have greatly impeded their commercial and therapeutic viability. Moreover, prior skilled artisans have been unable to determine or understand the source or cause of these failures, and have therefore been unable to achieve a systematically designed valve leaflet that overcomes these failures. Further, because these artisans were operating under the

constraint of the conventional wisdom and self-perpetuated dogma of the field, they were unable to deviate from valve leaflet shapes that had a belly and were focused on creating near vertical coaption surfaces.

15. In contrast, as described in the '612 application at paragraph 0056, my inventive valve leaflet does not require the use of geometric scaling and works equally well regardless of valve diameter or the height of the posts of the valve frame. Thus far, I have made and tested five different sizes of the claimed valve and all have performed equally well.

16. Moe states that analytical geometry was used to determine the leaflet shape disclosed therein. However, Moe also discredits prior art designs that used other shapes and combinations of shapes that can be described by analytical geometry, thereby teaching that not every analytical geometric shape or combination of shapes can meet even the criteria set forth by the conventional wisdom in the art.

17. There are virtually an infinite number of shapes and sizes of geometric shapes having various sizes that can be combined to form a valve leaflet so that a person operating under the teachings of the prior art could experiment indefinitely without arriving at a design that remedies the shortcomings of prior valves. Indeed, some skilled artisans have attempted to obtain improved valve leaflets by trial and error, but because they did not understand why some samples may have worked better than others, results were nearly impossible to replicate; any given sample could perform better or worse based on factors that the artisans may not have even considered or understood. Additionally, any such trial and error successes could not be successfully scaled up or down to other sizes because simple geometric scaling does not apply to the complex dynamics of a heart valve leaflet opening and closing and cyclically subjected to forward flow and reverse back-pressure at the rate of one or more cycles per second.

18. To the best of my knowledge, a commercial valve based on Moe's design was never produced. However, because the Moe valve has the characteristic dual-curvature belly of

prior art valves, the behavior of the Moe valve can be predicted with reasonable certainty based on my experience with other similar prior art valves.

19. The '612 application compares the design, performance, and stress characteristics of a prior art valve leaflet with the presently claimed valve leaflet. An embodiment of a prior art valve has been analyzed and tested for comparison with a valve including the claimed leaflets. The prior art valve embodiment was designed to have leaflets of a mathematically defined shape that allows good wash-out of the entire leaflet orifice, including the area close to the frame posts, to relieve the problem of thrombus deposition under clinical implant conditions. Depictions of the geometry, stress, and strain energy characteristics of the leaflets of the prior art valve embodiment are shown in the '612 application in Figures 2b, 4a, 4b, 5b, 7c, 7d, 8a, 8b, 8c, 8d, 11a, 11b, 11c, and 11d. The prior art valve embodiment has a leaflet that combines a generally elliptical upper portion with a generally conical lower portion such that a belly is formed at the transition between the upper and lower portions.

20. The valve leaflets of the prior art valve embodiment were designed with the view that the apposition of the leaflets in the commissural region is critical. The prior art valve embodiment also assumes that the maximum loads on the leaflets are those generated when the valve is closed, and that the highest stresses (which occur in the region of the commissures) can be reduced by making the belly of the leaflet as low as practicable in the closed valve, which requires that there must be sufficient material in the leaflet to allow the desired low closing. Thus, the prior art valve embodiment incorporates the conventional wisdom in a similar manner to the Moe valve and results in a valve leaflet with a belly that must invert every time the valve opens and closes.

21. An embodiment of the present claimed valve has been developed and produced by AorTech as the model M95C valve. Independent claim 16 and its dependent claims 17-23, as initially filed and as currently pending in the '612 application, cover the M95C valve that has been produced and tested as described herein.

22. When I began the process of developing the claimed valve leaflet, I recognized that nobody in the prior art had been able to determine the source or cause of the failures that had been seen in prior art artificial valve leaflets, and posited that if I were able to identify the source or cause of the failures, then I may be able to design a valve that is capable of avoiding the failure problems. I encountered tremendous resistance as those of experience in designing artificial heart valves did not embrace my novel and unconventional approach, which was not the approach they had taken or would have found obvious to take at that time.

23. In working to solve the problems of the prior art valve leaflets, I first proposed to conduct not only a static stress analysis of the valve leaflets in the closed and open positions, as had been done by prior artisans, but to develop the capability to dynamically model the stress, as well as the strain energy density, to which a valve leaflet would be subjected throughout each cycle of opening and closing. This had never been done before for artificial heart valve leaflets because it was not considered important or relevant to the design and operation of the valves. Indeed, I was told that such an analysis was unnecessary and would be fruitless, because it was already known that the maximum stresses on the valve leaflets occurred in the fully closed position.

24. The dynamic computer simulation model I developed, from scratch, uses finite element techniques and advanced numerical analysis to simulate stress concentrations, potential for crack growth, and fatigue resistance in a valve leaflet both under physiological conditions (i.e., an opening and closing cycle of about 1 Hz) and accelerated duty conditions (i.e., an opening and closing cycle of about 13 Hz). The dynamic model simulates the opening and closing of the valve leaflets in very small time increments to be able to predict and identify the location and intensity of stresses that can lead to crack propagation and valve leaflet failure. Still, to my knowledge, no artisans in this field are doing the type of dynamic modeling I have done. In discussing my dynamic simulation, reference will be made to Figs. A-1 through A-7D, which are appended hereto in Exhibit A. These figures are submitted in color and were shown to

the Examiner Jonathan R. Stroud and Primary Examiner Thomas J. Sweet in color during the Interview of March 25, 2009.

25. In order to better predict modes of failure, my dynamic simulation converts stress fields into maps of strain energy release, which can then be correlated with regions of the leaflet where a crack or defect is most likely to begin and propagate, and can be used to determine the initial direction of crack propagation.

26. An early application of my dynamic simulation model was to evaluate the prior art valve embodiment described above in paragraphs 19-20, and to predict any potential problems that might arise during laboratory and animal testing. As was discussed with Examiners Stroud and Sweet at the Interview of March 25, 2009, the tested prior art valve embodiment includes a belly very similar to that disclosed in Moe. My dynamic simulation showed clearly that every time the prior art valve embodiment opens and closes, each leaflet is subjected to highly concentrated stresses as the belly inverts, or pops through; when the valve is closed the leaflet belly is convex inward and when the valve is open the leaflet is concave inward, so that at an intermediate point, the excess material that forms the leaflet must buckle to invert its position in two directions, which causes very large stresses. As shown in my dynamic simulation, the buckling of the excess material as the belly inverts is very rapid and gives rise to regions of very intense strain energy release.

27. Subsequently, my dynamic simulation was used to evaluate the model M95C valve and to predict the absence of the high stresses and failure problems during opening and closing that had plagued prior art valves.

28. Fig. 8a of the '612 application shows the principal stress envelope of the prior art valve embodiment, Fig. 8b shows the strain energy release present in the X (lateral) axis of the prior art valve embodiment when the leaflet moves from a closed position to an open position, Fig. 8c shows the strain energy release present in the Y (axial) axis of the prior art valve

embodiment when the leaflet moves from a closed position to an open position, and Fig. 8d shows the combined strain energy release of the prior art valve embodiment when the leaflet moves from a closed position to an open position.

29. As shown in Figs. A-1A and A-1B, my dynamic simulation identifies a high strain energy density region in an upper middle portion of the leaflet of the prior art valve embodiment, which the simulation predicts will lead to rapid crack propagation in a lateral direction across the leaflet. (Note that the strain energy density map of Fig. A-1A corresponds to Fig. 8c in the originally filed '612 application.) Fig. A-2 is a photograph of a prior art valve embodiment that failed during laboratory testing in precisely the mode predicted by my dynamic simulation, with a lateral crack propagating across the leaflet.

30. As shown in Figs. A-3A and A-3B, my dynamic simulation further identifies a high strain energy density region along the upper free edge of the leaflet, which the simulation predicts will lead to rapid crack propagation in an axial direction downward into the leaflet. (Note that the strain energy density map of Fig. A-3A corresponds to Fig. 8b in the originally filed '612 application.) Fig. A-4 is a photograph of a prior art valve embodiment that failed during laboratory testing in precisely the mode predicted by my dynamic simulation, with an axial crack propagating downward from the free edge of the leaflet. A mapping of the strain energy density through an opening cycle of the prior art valve embodiment leaflet is also shown in Figs. 11a through 11d of the '612 application.

31. In contrast, Fig. 9a of the '612 application shows the principal stress envelope of the model M95C valve, Fig. 9b shows the strain energy release present in the X (lateral) axis of the model M95C valve when the leaflet moves from a closed position to an open position, Fig. 9c shows the strain energy release present in the Y (axial) axis of the model M95C valve when the leaflet moves from a closed position to an open position, and Fig. 9d shows the combined strain energy release of the model M95C valve when the leaflet moves from a closed position to

an open position. Figs. 9a-9d showing the claimed (model M95C) valve leaflet can be compared directly with Figs. 8a-8d showing the prior art valve embodiment leaflet.

32. As shown in Fig. A-5, my dynamic simulation shows the absence of a high strain energy density anywhere in the leaflet, and in particular in an upper portion of the leaflet, and accordingly the simulation predicts a lack of crack propagation across the leaflet. (Note that the strain energy density map of Fig. A-5 corresponds to Fig. 9c in the originally filed '612 application.) Testing (discussed below) has proven my dynamic simulation to be accurate in this regard.

33. As shown in Fig. A-6, my dynamic simulation shows the absence of a high strain energy density anywhere in the leaflet, and in particular along the upper free edge of the leaflet, and accordingly the simulation predicts a lack of crack propagation across the leaflet. (Note that the strain energy density map of Fig. A-6 corresponds to Fig. 9b in the originally filed '612 application.) Testing (discussed below) has proven my dynamic simulation to be accurate in this regard.

34. It can readily be seen that the peak stress concentration from the prior art valve leaflet (Fig. 8a) is no longer present in the claimed valve leaflet (Fig. 9a), and the locations of high strain energy density during opening and closing the valve leaflet are also no longer present (compare Figs. 9b-9d and A-5, A-6 with Figs. 8b-8d and A-1A, A-3A).

35. Fig. A-7A is a profile of the vertical midplane of the prior art valve embodiment leaflet in the cast position (which is approximately halfway between open and closed), taken along the centerline of the leaflet, showing the curvature that forms the belly. The valve of Moe has a similar profile, which can be seen generally in Moe Figs. 3 and 5. In the originally filed '612 application, Fig. 7d shows the profile of the vertical midplane of the prior art valve embodiment leaflet in the closed (I) and open (II) positions, clearly indicating the stress-inducing inversion of the belly between these two positions.

36. Fig. A-7B is a profile of the vertical midplane of the model M95C valve leaflet in the cast position (which is approximately halfway between open and closed), taken along the centerline of the leaflet, showing the nearly linear profile of the leaflet. In the originally filed '612 application, Fig. 7b shows the profile of the vertical midplane of the model M95C valve leaflet in the closed (I) and open (II) positions, clearly indicating no stress-inducing inversion between these two positions.

37. Fig. A-7D (which corresponds to Fig. 5a in the originally filed '612 application) shows the vertical midplane profile of the model M95C valve in the fully closed position, showing the substantially linear profile of the leaflet, as claimed. The shape of the leaflet when cast allows for slight flexure of the frame posts so that a substantially linear profile is achieved in the closed position.

38. Fig. A-7C is an overlay of the vertical midplane profiles of the prior art valve embodiment leaflet (shown in Fig. A-7A) and the model M95C valve leaflet (shown in Fig. A-7B), emphasizing the absence of a belly in the claimed valve leaflet.

39. Accelerated wear testing was conducted on the prior art valve embodiment. It should be noted that at 1 Hz, a typical heart beats over 100,000 beats per day (each beat corresponding to one opening and one closing of the heart valves) or about 40,000,000 beats per year. As noted above, accelerated wear testing is usually conducted at 13 Hz. The prior art valve embodiments exhibited a 15% failure rate, in a sample of over 100 valves, before reaching 50,000,000 cycles (equivalent to about 1.25 years). When the prior art valve embodiments failed, they did so catastrophically in the two failure mechanisms predicted by my dynamic simulation, either with a vertical crack propagating downward from the free edge of the leaflet (as in Fig. A-5), or with a lateral crack propagating outward from an upper middle portion of the leaflet belly (as in Fig. A-6).

40. Pre-clinical animal testing was conducted by implanting the prior art valve embodiments into sheep. In six-month studies, 3 out of 7 implanted valves failed, resulting in only a 57% survival rate.

41. Accelerated wear testing was conducted on the model M95C valve. In an initial test, the model M95C valves exhibited a 100% survival rate, in a sample of 30 valves, for more than 400,000,000 cycles (equivalent to more than about 10 years). In a follow-up test, the model M95C valves again exhibited a 100% survival rate, in sample of 30 valves, for 420,000,000 cycles (equivalent to about 10.5 years). Both tests were conducted at a pressure of 120mm Hg, which is a normal pressure exerted by a healthy human heart.

42. Further accelerated wear testing of the model M95C valve was conducted at higher pressures that were gradually stepped up. At the highest pressure setting of 400mm Hg (well above pressures normally exerted by a healthy human heart), the model M95C valve exhibited 100% survival after 200,000,000 cycles (equivalent to about 5 years).

43. Pre-clinical animal testing was conducted by implanting the model M95C valves into sheep. In six-month studies, all 15 implanted valves operated without problems, resulting in a 100% survival rate.

44. To further test my dynamic simulation and to compare the integrity of the prior art and claimed (model M95C) valves, initial cracks or defects were intentionally introduced into the valve leaflets, and accelerated wear testing was conducted. In some instances, the initial defects were introduced by pushing a suture needle through the leaflet and then withdrawing the suture needle from the leaflet, as might accidentally occur during surgery installing a valve into a heart. The ability of a valve leaflet to survive after this type of damage, at least for several days or weeks, may be critical in keeping a patient alive, because it is extremely undesirable to keep a patient on an artificial heart-lung machine long enough to replace a damaged valve during the

same surgery; therefore a damaged valve must be able to survive without failure until a second surgery can be performed to implant a new valve.

45. When a defect was introduced in the upper middle belly portion of the prior art valve embodiment leaflet, and the valve then subjected to accelerated wear testing, the leaflet failed almost immediately (e.g., in less than 100,000 cycles or one day). The defect rapidly propagated as predicted by my dynamic simulation.

46. When one or more defects were introduced into various portions of the model M95C leaflet, including locations corresponding to those locations on the prior art valve embodiment leaflet that resulted in nearly immediate failure, the model M95C operated normally with no propagation of the defect even after tens of millions of cycles (or the equivalent of several months).

47. In addition to the dramatic improvements in durability and survival of the model M95C as compared with the tested prior art valve embodiment (and other prior art valves), the model M95C valve also achieved the unexpected result of having a higher net forward flow of fluid therethrough because the shape of the model M95C leaflets enables the valve to open sooner in the cycle and more quickly than prior art valves. As shown in the originally filed '612 application at Fig. 13, the claimed leaflet without a belly opens with less pressure gradient than prior art valves having a belly, which allows a greater flow through the valve for the same pressure gradient. As depicted, the model M95C valve (shown as "23 mm new design" in Fig. 13) has a mean pressure gradient of between about 25% and 40% lower than that of the prior art valve embodiment (shown as "23mm" in Fig. 13). As a result, the model M95C valve has been shown to open more quickly and thus to allow up to 5% more flow therethrough on each beat of the heart than the prior art valve embodiment.

48. In addition, the model M95C valve has been shown to have coaption nearly as good as prior art valves, and closes more quickly than prior art belly valves, so that regurgitation

through the M95C valve is minimized. As a result, the net positive flow is up to 5% larger through the model M95C valve than through the prior art valve embodiment. In addition, any slight regurgitation through the model M95C valve may be beneficial because it prevents stagnation and lessens the chance of thrombus deposition where the leaflets adjoin the support posts.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code; and that willful false statements may jeopardize the validity of the application or any patent issuing thereon.

4/16/09
Date

Jason Gordon Beith

EXHIBIT A

- Fig. A-1A: Strain energy density map for the prior art valve embodiment leaflet in the Y (axial) direction during movement from a closed position to an open position.
- Fig. A-1B: Schematic showing the stress induced in the prior art valve embodiment leaflet and the predicted direction of initial crack propagation for a valve leaflet having a strain energy density map as in Fig. 1A.
- Fig. A-2: Photograph showing the catastrophic failure of a prior art valve embodiment leaflet subjected to strain energy density as in Fig. 1A.
- Fig. A-3A: Strain energy density map for the prior art valve embodiment leaflet in the X (lateral) direction during movement from a closed position to an open position.
- Fig. A-3B: Schematic showing the stress induced in the prior art valve embodiment leaflet and the predicted direction of initial crack propagation for a valve leaflet having a strain energy density map as in Fig. 3A.
- Fig. A-4: Photograph showing the catastrophic failure of a prior art valve embodiment leaflet subjected to strain energy density as in Fig. 3A.
- Fig. A-5: Strain energy density map for the model M95C (claimed) valve leaflet in the Y (axial) direction during movement from a closed position to an open position.
- Fig. A-6: Strain energy density map for the model M95C (claimed) valve leaflet in the X (lateral) direction during movement from a closed position to an open position.
- Fig. A-7A: Mid-profile of a prior art valve embodiment leaflet in the cast position, showing the belly formed by the transition from the lower portion to the generally vertical upper portion of the leaflet.
- Fig. A-7B: Mid-profile of a model M95C (claimed) valve leaflet in the cast position, showing a generally linear profile that eliminates the belly.
- Fig. A-7C: Overlay of the mid-profiles of Figs. 7A and 7B.
- Fig. A-7D: Mid-profile of a model M95C (claimed) valve leaflet in the closed position, showing a substantially linear profile to minimize strain energy.

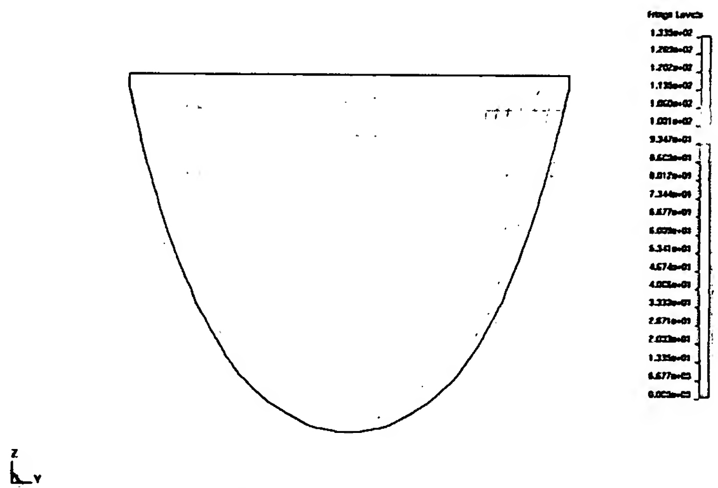

Fig A-1A

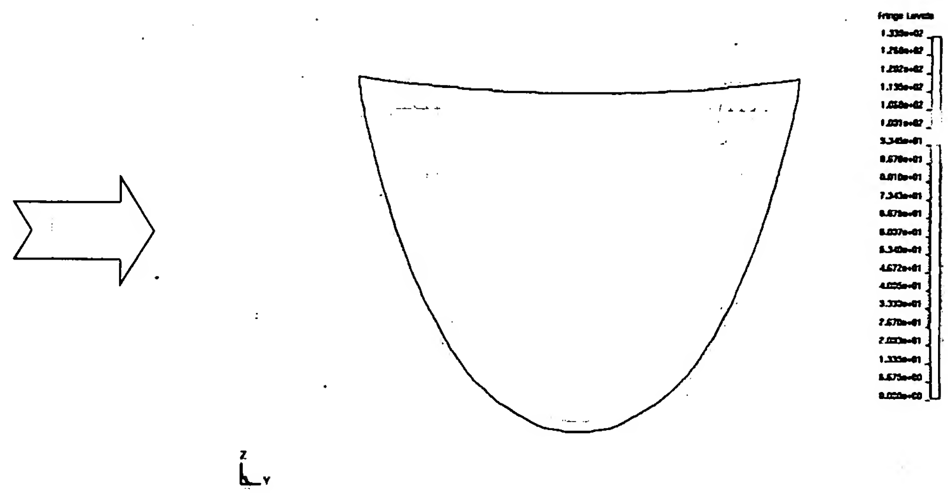

Fig A-5

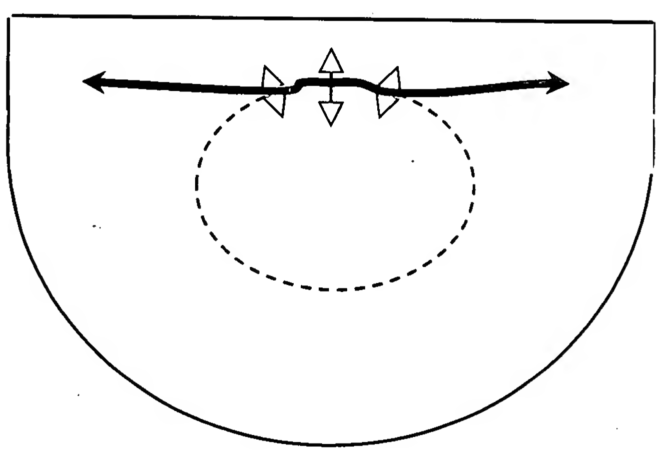

Fig A-1B

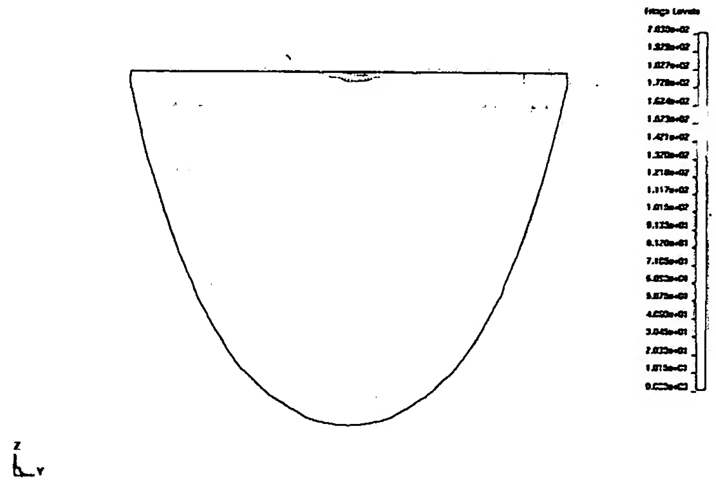

Fig A-3A

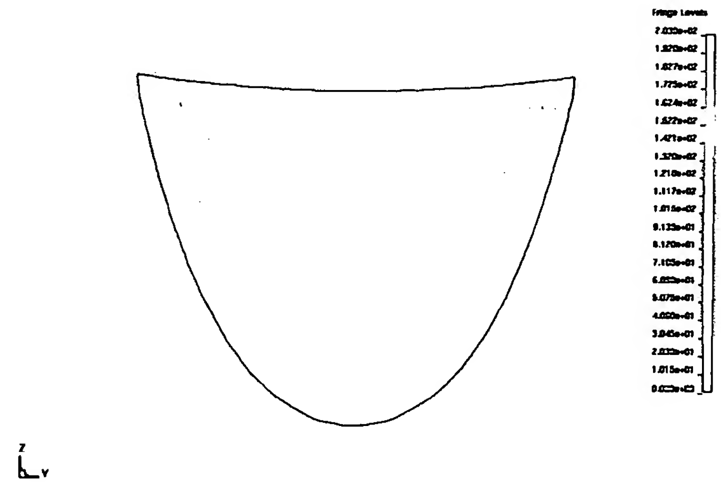

Fig A-6

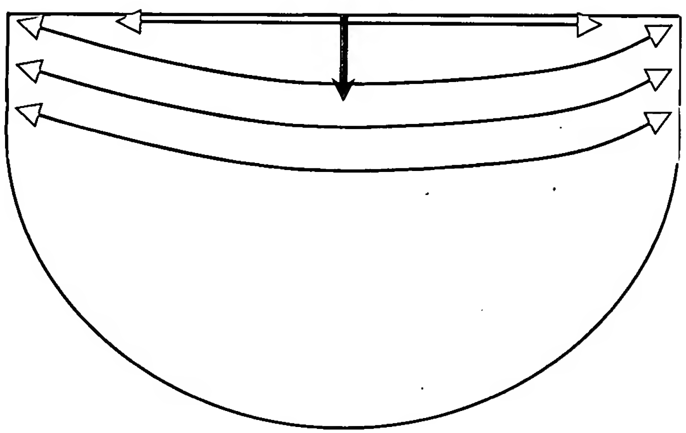

Fig A-3B

Fig A-2

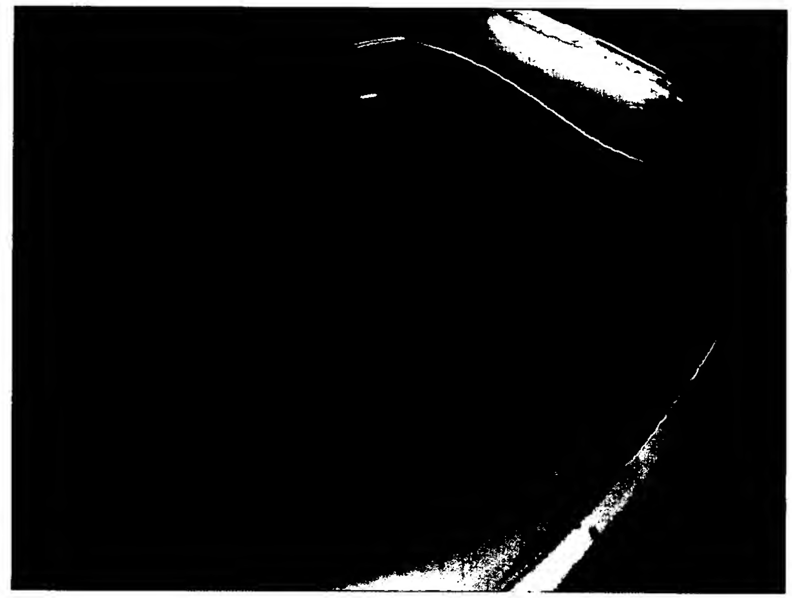

Fig A-4

Fig A-7A

Fig A-7B

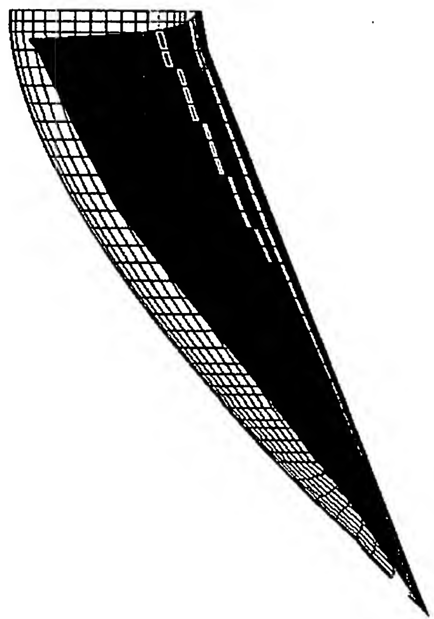

Fig A-7C

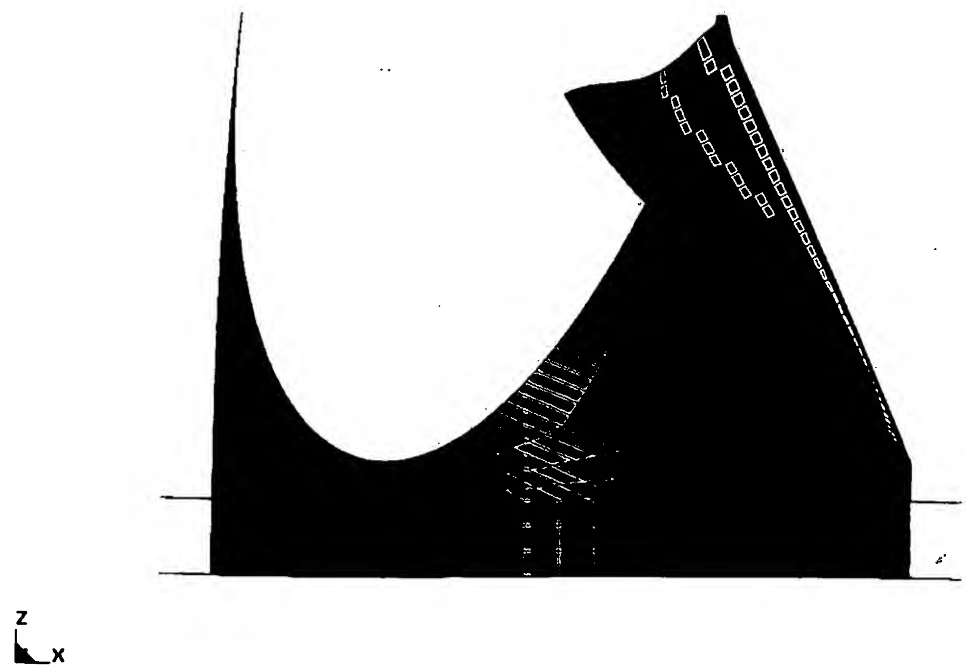

Fig A-7D